Abstract in English

Charles University in Prague
Faculty of Pharmacy in Hradec Králové
Department of pharmacology and toxicology
Candidate: Monika Šulcová MSc.
Consultant: Dr. Přemysl Mladěnka, Ph.D.
Name of thesis: Comparison of iron chelating activity of 8-hydroxyquinolines by direct spectrophotometry

Iron is a biogenic element needed for cell life. Excess iron can be very dangerous for the organism. Thus iron fate in the organism is meticulously regulated. The iron overload arises mainly as the result of frequent blood transfusion or some hematologic diseases. Toxicity of iron is based on the ability to catalyze the formation of reactive oxygen species. The risk can be reduced by the treatment with iron chelators. Iron chelators are compounds with different structures that are therapeutically used for iron intoxication, but are also examined in the treatment of neurodegenerative diseases, acute myocardial infarction and cancer. The ability to bind iron chelator depends not only on its structure, but also on pH.

The aim of this work was to compare iron-chelating activity of 8-hydroxyquinolines (basic substance and its derivatives - 5,7-dichloro derivative cloroxin and 5-chlor-7-iod derivative clioquinol) by direct spectrophotometry and to find out the stoichiometry of their complexes with ferrous/ferric ions at various pathophysiological important pHs (4,5-7,5).

It was found that all tested chelators from the groups of 8-hydroxyquinolines were almost equally effective, with the exception of ferrous ion chelation at pH 4,5. Basic substance 8-hydroxyquinoline was unable to form a complex with ferrous ions at this pH in contrast to its derivatives. Although clioquinol formed complex with ferrous iron under these conditions, the substance had likely relatively low affinity for iron. Cloroxin had at this conditions the highest affinity for ferrous ions from the tested substances, but the precise stoichiometric ratio (2:1 or 3:1) cannot be established with precision. In all other cases, cloroxin and 8-hydroxyquinoline formed complexes with iron in the ratio of 3:1, the substance: iron, respectively. It appeared that clioquinol similarly chelated iron in the ratio of 3:1 in all these cases, but this cannot be approved by use of this methodology.

In summary, the tested 8-hydroxyquinoline are strong chelators of ferric and ferrous ions with comparable activity even at lower pH. The only exception is ferrous ion chelation at pH 4,5, where the most appropriate seems to be the 5,7-dichlor derivative of the basic 8-hydroxyquinoline structure.